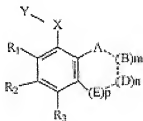


CLAIM AMENDMENTS

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims

1. (Amended) The use of A method of using a compound compounds of General Formula I



Formula I

wherein:

X represents O, S;

Y represents H or, along with X, where X = O, a carbohydrate radical;

A represents N or NR₄;

B represents CR₅, NR₅ or N;

D represents CR₆, NR₆ or N;

E represents CR₇, NR₇ or N;

with the condition that the ring containing group A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or double bond;

R₁, R₂, R₃, R₄, R₅, R₆ and R₇ each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C₁-C₆ alkyl, OH, C₁-C₆ polyhydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, (CH₂)_q-OR', wherein q is 1, 2 or 3, CF₃, CH₂-CH₂F, O-CH₂-CH₂F, CH₂-CH₂-CH₂F, CN, NO₂, O(CO)R', OR', SR', COOR' -SO₃H, (CH₂)_r-CO₂R'', (CH₂)_r-CO-R', wherein r is 1, 2 or 3 and R_{ph}, wherein R_{ph} represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R₁-R₇ except for a phenol group;

R' is H or a C₁₋₃ alkyl group;

R'' is H, a C₁-C₆ alkyl group or a C₁-C₆ alkoxy group;

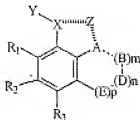
with the condition that only one of R₁, R₂, R₃, R₄, R₅, R₆, R₇, X and Y is or has a radioactive isotope;

said method comprising:

in the preparation of preparing a composition containing said compound of General Formula 1 for diagnosis and/or monitoring of diseases associated with the formation of amyloid protein fibrils, particularly those that appear as amyloid plaques and affect the central nervous system; and

optionally administering said composition to a subject and detecting amyloid protein fibrils based on uptake of said compound of General Formula I.

2. (Amended) ~~The use of A~~ A method of using a compound compounds
of General Formula II.



Formula II

wherein:

X represents O, S;

Y represents H or, along with X, where X = O, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the | | | | | line represents a coordinate bond;

A represents N or NR₄;

B represents CR₅, NR₅ or N;

D represents CR₆, NR₆ or N;

E represents CR₇, NR₇ or N;

with the condition that the ring containing substituent A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or double bond;

R₁, R₂, R₃, R₄, R₅, R₆ and R₇ each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C₁-C₆ alkyl, OH, C₁-C₆ polyhydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, (CH₂)_q-OR', wherein q is 1, 2 or 3, CF₃, CH₂-CH₂F, O-CH₂-CH₂F, CH₂-CH₂-CH₂F, CN, NO₂, O(CO)R', OR', SR', COOR' -SO₃H, (CH₂)_r-CO₂R'', (CH₂)_r-CO-R', wherein r is 1, 2 or 3 and R_{ph}, wherein R_{ph} represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R₁-R₇ except for a phenol group;

R' is H or a C₁₋₃ alkyl group;

R'' is H, a C₁-C₆ alkyl group or a C₁-C₆ alkoxy group;

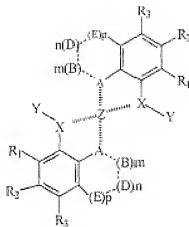
with the condition that only one of R₁, R₂, R₃, R₄, R₅, R₆, R₇, X, Y or Z is or has a radioactive isotope;

said method comprising:

in the preparation of preparing a composition containing said compound of General Formula II for diagnosis and/or monitoring of diseases associated with the formation of amyloid protein fibrils, particularly those that appear as amyloid plaques and affect the central nervous system; and

optionally administering said composition to a subject and detecting amyloid plaques based on uptake of said compound of General Formula II.

3. (Amended) ~~The use of~~ A method of using a compound compounds of General Formula III.



Formula III

wherein:

X represents O, S;

Y represents H or, along with X, where $X = O$, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the ||||| line represents a coordinate bond:

A represents N or NR₄:

B represents CR₅, NR₅ or N;

D represents CR₆, NR₆ or N;

E represents CR₇, NR₇ or N;

with the condition that the ring containing substituent A has a

maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where $m + n + p = 2$ or 3;

the dashed lines - - - represent a single or double bond;

R₁, R₂, R₃, R₄, R₅, R₆ and R₇ each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C₁-C₆ alkyl, OH, C₁-C₆ polyhydroxyalkyl, C₁-C₆ alkoxyl, C₁-C₆ alkoxyalkyl, (CH₂)_q-OR', wherein q is 1, 2 or 3, CF₃, CH₂-CH₂F, O-CH₂-CH₂F, CH₂-CH₂-CH₂F, CN, NO₂, O(CO)R', OR', SR', COOR' -SO₃H, (CH₂)_r-CO₂R'', (CH₂)_r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R₁-R₇ except for a phenol group;

R' is H or a C₁₋₃ alkyl group;

R'' is H, a C₁-C₆ alkyl group or a C₁-C₆ alkoxy group;

with the condition that only one of R₁, R₂, R₃, R₄, R₅, R₆, R₇, X, Y or Z is or has a radioactive isotope;

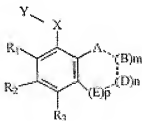
said method comprising:

in the preparation of preparing a composition containing said compound of General Formula III for diagnosis and/or monitoring of diseases associated with the formation of amyloid protein fibrils, particularly those that appear as amyloid plaques and affect the central nervous system; and

optionally administering said composition to a subject and detecting amyloid plaques based on uptake of said compound of General Formula III.

4. (Original) Use according to claims 1, 2 and 3 for diagnosis and/or monitoring in animals, transgenic animals, and particularly in humans, of diseases such as Alzheimer's, Parkinson's, Huntington, cystic fibrosis, late onset diabetes, motor neuron disease, Mediterranean fever, Muckle-Wells syndrome, idiopathic myeloma, amyloid polyneuropathy, amyloid cardiomyopathy, senile systemic amyloidosis, hereditary cerebral haemorrhage with amyloidosis, Down syndrome, Creutzfeld-Jacob disease, Kuru, Gerstmann-Straussler-Schienenker syndrome, thyroid medullar carcinoma, amyloid valve deposits, amyloidosis in dialysis patients, inclusion body myositis, amyloid muscular deposits, Sickie Cell Parkinson anaemia, type 2 diabetes, amongst others.

5. (Original) Compounds of General Formula I



Formula I

wherein:

X represents O, S;

Y represents H or, along with X, where $X = O$, a carbohydrate radical;

A represents N or NR_4 ;

B represents CR_5 , NR_5 or N;

D represents CR_6 , NR_6 or N;

E represents CR_7 , NR_7 or N;

with the condition that the ring containing substituent A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where $m + n + p = 2$ or 3;

the dashed lines - - - represent a single or double bond;

R_1 , R_2 , R_3 , R_4 , R_5 , R_6 and R_7 each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C_1 - C_6 alkyl, OH, C_1 - C_6 polyhydroxyalkyl, C_1 - C_6 alkoxyl, C_1 - C_6 alkoxyalkyl, $(CH_2)_q$ -OR', wherein q is 1, 2 or 3, CF_3 , CH_2 - CH_2F , O - CH_2 - CH_2F , CH_2 - CH_2 - CH_2F , CN, NO_2 , $O(CO)R'$, OR', SR', $COOR' - SO_3H$, $(CH_2)_r$ - CO_2R'' , $(CH_2)_r$ -CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R_1 - R_7 except for a phenol group;

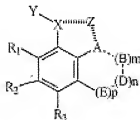
R' is H or a C_{1-3} alkyl group;

R'' is H, a C_1 - C_6 alkyl group or a C_1 - C_6 alkyloxy group;

with the condition that R₁, R₂, R₃, R₄, R₅, R₆, R₇, X and Y are not all simultaneously H, and

with the condition that only one of R₁, R₂, R₃, R₄, R₅, R₆, R₇, X and Y is or has a radioactive isotope;

6. (Original) Compounds of General Formula II



Formula II

wherein:

X represents O, S;

Y represents H or, along with X, where X = O, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the ||||| line represents a coordinate bond;

A represents N or NR₄;

B represents CR₅, NR₅ or N;

D represents CR₆, NR₆ or N;

E represents CR₇, NR₇ or N;

with the condition that the ring containing group A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where $m + n + p = 2$ or 3;

the dashed lines - - - represent a single or double bond;

R₁, R₂, R₃, R₄, R₅, R₆ and R₇ each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C₁-C₆ alkyl, OH, C₁-C₆ polyhydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, (CH₂)_q-OR', wherein q is 1, 2 or 3, CF₃, CH₂-CH₂F, O-CH₂-CH₂F, CH₂-CH₂-CH₂F, CN, NO₂, O(CO)R', OR', SR', COOR' -SO₃H, (CH₂)_r-CO₂R'', (CH₂)_r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R₁-R₇ except for a phenol group;

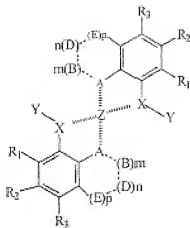
R' is H or a C₁₋₃ alkyl group;

R'' is H, a C₁-C₆ alkyl group or a C₁-C₆ alkyloxy group;

with the condition that R₁, R₂, R₃, R₄, R₅, R₆, R₇, X and Y are not all simultaneously H, and

with the condition that only one of R₁, R₂, R₃, R₄, R₅, R₆, R₇, X, Y or Z is or has a radioactive isotope;

7. (Original) Compounds of General Formula III



Formula III

wherein:

X represents O, S;

Y represents H or, along with X, where X = O, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the ||||| line represents a coordinate bond;

A represents N or NR₄;

B represents CR₅, NR₅ or N;

D represents CR₆, NR₆ or N;

E represents CR₇, NR₇ or N;

with the condition that the ring containing group A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where $m + n + p = 2$ or 3;

the dashed lines - - - represent a single or double bond;

R₁, R₂, R₃, R₄, R₅, R₆ and R₇ each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C₁-C₆ alkyl, OH, C₁-C₆ polyhydroxyalkyl, C₁-C₆ alkoxyl, C₁-C₆ alkoxyalkyl, (CH₂)_q-OR', wherein q is 1, 2 or 3, CF₃, CH₂-CH₂F, O-CH₂-CH₂F, CH₂-CH₂-CH₂F, CN, NO₂, O(CO)R', OR', SR', COOR' -SO₃H, (CH₂)_r-CO₂R'', (CH₂)_r-CO-R', wherein r is 1, 2 or 3 and R_{ph}, wherein R_{ph} represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R₁-R₇ except for a phenol group;

R' is H or a C₁₋₃ alkyl group;

R'' is H, a C₁-C₆ alkyl group or a C₁-C₆ alkyloxy group;

with the condition that only one of R₁, R₂, R₃, R₄, R₅, R₆, R₇, X, Y or Z is or has a radioactive isotope;

and with the condition that when

A is N,

B, D and E are all CH,

X is O, and

m, n and p are all 1,

then R₁, R₂ and R₃ are not all H.

8. (Original) Compounds according to claim 5, characterised by being:

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline

5-[¹²³I]iodo-7-iodo-8-hydroxyquinoline

5-iodo-7-[¹²³I]iodo-8-hydroxyquinoline

5-[¹²⁴I]iodo-7-iodo-8-hydroxyquinoline

5-iodo-7-[¹²⁴I]iodo-8-hydroxyquinoline

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline

5-chloro-7-iodo-8-[¹¹C]methoxyquinoline

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline glucuronide

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline glucuronide

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline glucuronide

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline glucuronide

5-chloro-7-iodo-8-[¹¹C]methoxyquinoline glucuronide

5-[¹²³I]-8-hydroxyquinoline

5-[¹²⁴I]-8-hydroxyquinoline

7-[¹²³I]-8-hydroxyquinoline

7-[¹²⁴I]-8-hydroxyquinoline

5-[¹⁸F]-8-hydroxyquinoline

5-[¹⁸F]-8-hydroxyquinoline

9. (Original) Compounds according to claim 6:

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Fe(II) complex

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Cu(II) complex

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Zn(II) complex

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Mn(II) complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Fe(II) complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Cu(II) complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Zn(II) complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Mn(II) complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Fe(II) complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Cu(II) complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Zn(II) complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Mn(II) complex

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Fe(II) complex

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Cu(II) complex

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Zn(II) complex

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Mn(II) complex

5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Fe(II) complex

5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Cu(II) complex

5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Zn(II) complex

5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Mn(II) complex

5-chloro-7-iodo-8-hydroxyquinoline ^{99m}Tc complex

5-chloro-7-iodo-8-hydroxyquinoline ¹¹¹In complex

5-chloro-7-iodo-8-hydroxyquinoline ²⁰¹Tl complex

5-chloro-7-iodo-8-hydroxyquinoline ⁶⁷Ga complex

5-chloro-7-iodo-8-hydroxyquinoline ⁶⁸Ga complex

5-chloro-7-iodo-8-hydroxyquinoline ⁶⁷Cu complex

5-chloro-7-iodo-8-hydroxyquinoline ⁶⁴Cu complex

10. (Original) Compounds according to claim 7:

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Fe(II) bis-chelate complex

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Cu(II) bis-chelate complex

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Zn(II) bis-chelate complex

5-chloro-7-[¹²³I]iodo-8-hydroxyquinoline Mn(II) bis-chelate complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Fe(II) bis-chelate complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Cu(II) bis-chelate complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Zn(II) bis-chelate complex

5-chloro-7-[¹²⁴I]iodo-8-hydroxyquinoline Mn(II) bis-chelate complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Fe(II) bis-chelate complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Cu(II) bis-chelate complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Zn(II) bis-chelate complex

5-chloro-7-[¹⁸F]fluoro-8-hydroxyquinoline Mn(II) bis-chelate complex

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Fe(II) bis-chelate complex

5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Cu(II) bis-chelate complex
5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Zn(II) bis-chelate complex
5-[¹⁸F]fluoro-7-iodo-8-hydroxyquinoline Mn(II) bis-chelate complex
5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Fe(II) bis-chelate complex
5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Cu(II) bis-chelate complex
5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Zn(II) bis-chelate complex
5-chloro-7-iodo-8-[¹¹C]methoxyquinoline Mn(II) bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ^{99m}Tc bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ¹¹¹In bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ²⁰¹Tl bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ⁶⁷Ga bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ⁶⁸Ga bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ⁶⁷Cu bis-chelate complex
5-chloro-7-iodo-8-hydroxyquinoline ⁶⁴Cu bis-chelate complex

11. (Original) A pharmaceutical composition for diagnosis of diseases associated with protein deposition in the central nervous system comprising one of the compounds defined in claims 5 to 9.

12. (Original) A method for preparing the compounds defined in claims 5 and 8 comprising:

a) making a quinoline derivative react with an electrophilic aromatic

halogenation reagent incorporating a radioactive halogen atom, or

- b) making a quinoline derivative react with a radioactive halogenated derivative to effect an aromatic nucleophilic substitution reaction.

13. (Original) A method for preparing the compounds defined in claims 6 and 9 comprising:

- a) making a quinoline derivative react with a metal or rare earth cation,
- or,
- b) making a quinoline derivative react with a radioactive isotope of these elements

such that the metal or rare earth cation or the radioactive isotope of these elements is in a suitable oxidation state so as to produce the corresponding chelating product defined in claims 6 and 9.

14. (Original) A method for preparing the compounds defined in claim 7 comprising making a quinoline derivative react with:

- a) a metal or rare earth cation, or,
- b) a radioactive isotope of these elements.

in a suitable oxidation state so as to produce the corresponding chelating product defined in claims 7 and 10.

15. (New) The method of claim 1, wherein the amyloid protein fibrils

appear as amyloid plaques and affect the central nervous system.

16. (New) The method of claim 2, wherein the amyloid protein fibrils appear as amyloid plaques and affect the central nervous system.

17. (New) The method of claim 3, wherein the amyloid protein fibrils appear as amyloid plaques and affect the central nervous system.